on a large scale to confirm this work. Nevertheless, if the findings of these workers should be definitely confirmed, then intradermal tests in trichinous pigs would be just as specific as tuberculin tests in tuberculous cows. The opinion that has been held in the past, that we must have trichiniasis because of the inability to detect infested swine, would then be tenable no longer.

E. M. Butt, M.D. (University of Southern California School of Medicine, Los Angeles).—Our attention has been drawn to the subject of trichinosis by the startling figures obtained by a few recent workers in determining the prevalence of trichina infestation in cadavers. These figures are from widely separated localities and, excepting the report from New Orleans, indicate an incidence of trichina infestation in well over 15 per cent of the cadavers examined. Yet, as McNaught has pointed out, the vital statistics of the State of California show a very low incidence of the disease. This discrepancy has been dismissed quickly with the conclusion that, clinically, the disease is rare, and that subclinical infestation is common. However, quantitative evaluation of infestations would indicate that such an inference is not true in a certain percentage of positive cases. It follows, therefore, that patients with trichinosis are not seen medically or that our training and diagnostic methods are faulty and require scrutiny. Aside from the clinical importance of trichinosis, there is a public health aspect of utmost interest.

Recently, we have completed the examination of 150 diaphragms by the digestion method. These specimens have been taken at random from our autopsy service. The total percentage of positive findings was 17.3 per cent. Further analysis of these figures revealed a higher percentage of infestation in females than in males. This is due to the high incidence of trichina in diaphragms of colored females, a figure which in our small series was close to 50 per cent. Thirty-seven per cent of the diaphragms from Mexicans and Negroes, both males and females, were positive for trichinae.

It is still too early to adequately evaluate the diagnostic importance of the skin test. The few clinical cases that we have seen have all given an immediate positive reaction to the antigen. However, there are reports in the literature that indicate that such is not always the case. Furthermore, positive skin tests have been obtained in individuals with Trichuris trichiura infestation. So far, little attention has centered around the trichina skin test in hyperergic patients. These and other aspects must be taken into account before the skin test can be considered reliable in the diagnosis of trichinosis.

Trichinosis is a subject of considerable clinical and public health importance. Doctor McNaught's admirable paper should help to create more interest in the subject.

SNAKE VENOM: ITS USE IN POSTOPERATIVE HEMORRHAGE OF THE EYE*

By W. F. Swett, M.D.
San Francisco

Discussion *by Warren D. Horner, M. D., San Francisco; Frederick C. Cordes, M. D., San Francisco.*

THE management of postoperative hemorrhage, following major procedures on the eye, is always difficult to control, and the usual procedures are notoriously ineffective. These cases have always been a source of worry, and in my effort to find something to control this situation I was encouraged by reports of Peck [1] (1931), McFarlande and Barnett [2] (1934), and Dack [3] (1935), in their use of moccasin venom in the treatment of hemorrhagic disease.

During the past year I have had several stubborn postoperative hemorrhage cases which were responsible in my using the snake venom therapy, in an effort to find a good postoperative treatment in this distressing complication.

MOCCASIN VENOM

The moccasin venom was prepared in a concentration of 1/3000, in a physiological saline solution with 1/10,000 merthiolate being added as a preservative. According to these authors, it was efficacious in functional uterine bleeding, epistaxis, and hematuria in the Henoch-Schönlein syndrome, in thrombocytopenic purpura, in multiple heredity telangiectasis, and in hemoptysis from bronchiectatic cavities. The more recent applications have shown that the venom is excellent as a coagulent in local intractible bleeding, and was found especially effective in cases of functional uterine bleeding and idiopathic nasal hemorrhages. This led to its being used preoperatively, in patients predisposed to excessive hemorrhage, with equally good results. Hemophitic blood, which normally clotted in twenty to forty-five minutes, was clotted in seventeen seconds by a 1/10,000 dilution of venom, and has been used successfully in managing hemophiliac hemorrhages following dental extraction, tonsillectomy, epistaxis, and oozing from abdominal wounds.

In giving the venom, ecchymosis may develop at the site of injection in the first twenty-four hours, and most patients develop a reaction of hypersensitivity in approximately ten to fourteen days; however, the reaction is always local, and characterized by a hot, tender swelling at the point of injection only. No general reaction may be feared. In the six cases that I have used it on up to date, I have had no reaction whatever, either local or general.

The continuous oozing of blood from the iris or the wound into the anterior chamber, following cataract extractions, prolongs the healing and in many instances results in the failure of the wound to close, or even a painful eye with rupture of the wound and prolonged seepage from the anterior chamber.

In the first case, hemorrhage occurred the first day following operation and continued to ooze in spite of all treatment for ten days. I decided to use the moccasin venom put out by Lederle, and was very pleasantly surprised when the oozing stopped immediately after the first injection of .4 cubic centimeter. As soon as the hemorrhage was checked, the blood disappeared rapidly from the anterior chamber and the wound was closed completely four days later. I have used it in four cases since with identical results. These results have been so satisfying that I have come to look upon the venom as indispensable in the control of postoperative hemorrhage. To date I have only administered it in those cases which showed a tendency to hemorrhage after operation, and found that .5 cubic centimeter given daily for one week has been sufficient. I feel that the ideal method of use would be to give these injections previous to operation to prevent the complications rather than to correct them. I have not gone into this phase of the subject because I first wanted to demonstrate to my satisfaction the action of the venom on actively hemorrhaging cases.

* Read before the Eye, Ear, Nose, and Throat Section of the California Medical Association at the sixty-sixth annual session, May 2–6, 1937.

In one case of a severe iridocyclitis, accompanied by hemorrhage in the anterior chamber, I gave .5 cubic centimeter subcutaneously and have found that it also stopped the bleeding in the face of a severe inflammation in which no operation had been performed.

IN CONCLUSION

I am convinced that the most important point in the use of venom in postoperative hemorrhage is to give it in large enough doses to rapidly control the bleeding, and as it is not continued long enough to produce sensitization, this point need not be feared. The patients tolerate .1 cubic centimeter daily up to fourteen days if necessary, without any untoward symptoms.

In two other cases I used a dosage of .1 cubic centimeter daily for four days without any signs of hypersensitivity or local reaction.

In this small series of six cases, I believe I have demonstrated that moccasin venom has a definite place in the control of postoperative bleeding, and also has possibilities as a prophylactic procedure which may be used in intra-ocular surgery, particularly in cases where we are suspicious of having postoperative bleeding.

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DISCUSSION

WARREN D. HORNER, M.D. (384 Post Street, San Francisco).—A snake swallows its food whole, and what could be handier for a snake than a hypodermic injection ready at all times to paralyze its prey and to assist in its digestion! This is precisely what a venomous snake has. The venom is secreted in glands homologous with the mammalian salivary parotid. It is led down to fangs which are either grooved or hollow and so placed as to pierce the thing bitten. The act of biting contracts the temporal muscle, which exerts pressure over the poison gland which forces the venom to the fangs.

The toxic action of venoms varies enormously among the different snakes.

A large group of venoms, such as those of the Indian cobra and Australian death adder, act like curare in paralyzing skeletal muscles, and death may take place from paralysis of the muscles of respiration.

Another group, chiefly of the viper family, causes death by peripheral circulatory failure.

A third group causes death by the rapid coagulation of the victim's blood, due to the presence of thrombin or kinase in the venom, which set off the clotting reaction.

Other venoms contain anticoagulating substances thought to be antikinase or antithrombin. Hence, venom from the cobra, Australian copperhead or death adder causes blood to become incoagulable, either *in vivo* or *in vitro*.

Since we are interested alone in coagulating effects, we will discuss this phase further.

As early as 1893 Martin pointed out that certain snake venoms caused intravascular clotting.

In 1903, Lamb found that citrated blood could be clotted by particular venoms.

McFarlane and Barnett,[1] in 1934, found that a 1:10,000 dilution of viper venom could be sterilized by a Birkefeld filter, was not toxic in this dilution, and had coagulating powers even in hemophilia. This dilution has been used ever since in St. Bartholomew's Hospital, London, particularly in dental extractions, tonsillectomies, oozing of viscera, such as kidney and liver, and prostatectomies.

In America, since 1931, Peck[2] has advocated the use of moccasin venom and, with Lederle, has given us a commercial supply.

Rosenfeld and Lenke (1935) have used venom of the Australian tiger snake as a hemostatic.

The exact rôle of viper venom in the process of blood coagulation has been studied.

As you remember, the clotting of normal blood follows this scheme: Prothrombin in the plasma, plus calcium salts in the plasma, plus thrombokinase or injured-tissue juice, yields thrombin, which reacts with fibrinogen in the plasma to form fibrin or clot.

Indian and Australian viper venoms contain substances which are the equivalent of a mixture of thrombokinase and calcium, which can generate thrombin and set off the clotting mechanism.

Peck and Rosenthal attribute the coagulating effect of moccasin venom either to some effect on the blood-vessel walls or on the clotting factor of the blood.

Snake venom for antihemorrhagic purposes has been given a successful trial both in London and America. Its use to prevent hemorrhage in the eye is, as far as I can determine, original with Doctor Swett, for I noted no other reference relative to its employment in ophthalmology.

There are many cases in eye surgery where the fear of bleeding or recurrence of bleeding literally haunts one. Furthermore, we have only feeble means to prevent hemorrhage, even when we fear it preoperatively. I have never felt confident that calcium or horse serum, or anything else for that matter, could be depended upon.

In snake venom we have a promising new reagent which is worthy of our trial, and we are indebted to Doctor Swett for bringing this remedy to our attention.

❦

FREDERICK C. CORDES, M.D. (384 Post Street, San Francisco).—Doctor Swett has called to our attention a therapeutic measure that has a definite place in our armamentarium. It offers a rapid and effective means of controlling hemorrhage in certain cases.

The control of hemorrhage comes briefly under three headings: (1) Measures to remedy any underlying constitutional cause, such as scurvy. (2) Steps to prevent the flow of blood from the bleeding vessel by the application of direct pressure, or substances that contract the vessels. (3) Consolidation of the blood.

It is primarily with the third that we are concerned in the discussion of snake venom. According to Huggett,[3] the main coagulants used in medicine may be listed in five physiological classes.

1. Thrombokinases, such as tissue or platelet extracts, preparations of brain tissue or cephalin itself.
2. Thrombin preparations.
3. Calcium variants, such as calcium salts or parathyroid extract.
4. Proteins. Foreign proteins, peptone, and the blood sera of animals have been used.
5. Physical means; carbon dioxid inhalations, extreme heat, and styptics.

The use of snake venom comes under the head of treatment with thrombins, as it has been shown that venom, particularly that of vipera russellii, contains a highly active thrombin. In addition to being a powerful coagulant, venom also produces a very strong clot. The rapidity of action is most dramatic, as Doctor Swett has stated. From the above it follows that in those cases where the bleeding results from an abnormality of the blood itself, one can expect help from the use of snake venom.

In addition to the type of case mentioned by Doctor Swett, the prophylactic use of snake venom suggests itself in those cases of apparently simple contusion of the eyeball that develop severe vitreous hemorrhages, three to five days after the injury.

I feel that this paper is of particular significance, as it is, to the best of my knowledge, the first report of the use of snake venom in ophthalmology, and one of a very few instances of the use of venom reported in the American literature.

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2 Peck: Treatment, J. A. M. A., 105:413 (Aug.), 1935.

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